REMARKS

In response to the Office Action of January 29, 2003, Applicants have amended the claims, which when considered with the remarks herein, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

The examiner has made final the restriction requirement imposed earlier. Accordingly, claims 3, 9-24 and 30-32 have been withdrawn from consideration. Claims 1, 2, 4-8, 25-29 and 33-36 are presently pending in the present application.

Claims 33 -36 are objected to due to the claims depending from claim 3 which has been withdrawn. As presently amended, Claims 33-36 depend from claims 1 and 2 only. Withdrawal of the objection to claims 33-36 is therefore respectfully requested.

Claims 1-2, 4 -8, 25-29 and 33-36 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly violative of the written description requirement. According to the Examiner, the rejected claims do not recite the specific identity or function of any particular SH2A nucleotide sequence or protein and therefore a critical element of the invention remains undefined, such that the invention is not adequately described. The Examiner acknowledges that there is adequate written description for the cDNA sequence of SEQ ID NO: 1 obtained from submerged rice roots, which sequence encodes a polypeptide having an amino acid sequence of SEQ ID NO: 2, and said polypeptide having amino acid sequence homology to putative proteins and ORFs of a number of ESTs corresponding to hypothetical proteins of other plants, animals and fungi, as well as to bacterial proteins. The Examiner has taken the position that the

specification does not describe or characterise other DNA sequences corresponding to an SH2A or SH2A-like gene. January 20, 2003 Office Action, page 3.

Applicants respectfully traverse the rejection and submit the following. In the first instance, claims 1 and 2 are presently amended to recite in relevant part: "a transgenic plant having an altered ethylene response." Support for this amendment may be found throughout the specification, e.g., Example 6.

In addition, the specification provides ample written description for other DNA sequences corresponding to an SH2A or SH2A-like genes other than those exemplified in the text of the description. Thus, in addition to the exemplified nucleic acid sequences from rice (*Oryza sativum*), the specification teaches that other SH2A-like genes from other organisms may be used in the present invention. *No less than 26 sequences for other SH2A-like genes are described.* For example, on page 22, lines 24-26 of the specification, there is provided "[I]n yet another embodiment of the invention, there is provided an isolated nucleic acid coding for SH2A having the amino acid sequence as set forth in SEQ ID NO:2."

Page 23, paragraphs 1-4 teach the following:

> The present invention also provides isolated nucleic acids coding for SH2A homologs and the corresponding amino acids from such plants as tomato (*Lycopersicon esculentum*), soybean (*Glycine max*), and cotton (*Gossypium hirsutum*). The nucleotide sequence for a first SH2A-like gene from tomato is set forth in SEQ ID NO: 5. The amino acid sequence for the corresponding tomato SH2A homolog is set forth in SEQ ID NO:6. A nucleotide sequence for a second SH2A-like gene from tomato is set forth in SEQ ID NO:7. SEQ ID NO:8 sets forth the corresponding amino acid sequence for a second SH2A-like gene from tomato.
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> The nucleotide sequence for an SH2A-like gene from soybean is set forth in SEQ ID NO: 9. The amino acid sequence for the corresponding soybean SH2A homolog is set forth in SEQ

ID NO:10. The nucleotide sequence for a cotton SH2A-like gene is set forth in SEQ ID NO:11 while the corresponding amino acid sequence is set forth in SEQ ID NO:12.

Also provided are nucleotide sequences for human, mouse and zebrafish SH2A-like genes and the corresponding amino acid sequences. The nucleotide sequence for a human SH2A-like gene is set forth in SEQ ID NO:13. The corresponding amino acid sequence is set forth in SEQ ID NO:14. The nucleotide sequence for a mouse SH2A-like gene is set forth in SEQ ID NO:15 while the corresponding amino acid sequence is set forth in SEQ ID NO:16.

The nucleotide sequence for a zebrafish SH2A-like gene is set forth in SEQ ID NO:17. The corresponding amino acid sequence is set forth in SEQ ID NO:18.

Further, additional SH2A-like genes for use in the present invention are taught on page 28, last paragraph to page 29, first paragraph, of the specification:

In addition to the nucleotide sequences provided herein as SEQ ID NOs:1-18, other nucleotide sequences for SH2A-like genes and corresponding amino acid sequences which are useful in the practice of the present invention are provided on the genetic sequence databases such as EMBL and GenBank. For example, a nucleotide sequence for a second SH2A-like gene in soybean is provided by the accession AI441185 from the Genbank data base. A nucleotide sequence for an SH2A-like gene in cabbage is provided by accession L38235 from the Genbank data base. An SH2A-like gene nucleotide sequence in corn (*Zea mays*) is provided by accession AI649530 from the Genbank data base. Accession AI054437 from the Genbank data base provides the nucleotide sequence for an Iceplant (*Mesembryanthemum crystalllinum*) SH2A-like gene. Accession AT000213 from the DDBJ data base provides the nucleotide sequence for an SH2A-like gene in apple (*Malus domestica*). The nucleotide sequence for an SH2A-like gene in pine (*Pinus taeda*) is provided on the Genbank database by accession AI813053. Accession AI727947 on the Genbank database provides the nucleotide sequence for a second SH2A-like gene in cotton. Four accessions related to four

SH2A-like genes in *Arabidopsis thaliana* are also available as accessions N38691, N96935, T76549 and AC002505 on the Genbank database and correlate to the ATH1, ATH2, ATH4, and ATH3 genes respectively, as described herein.

Further, page 30, lines 1-17 provide:

Accession AI417749 from the Genbank data base provides the nucleotide sequence for a second human SH2A-like gene. A rabbit SH2A-like gene sequence is provided by accession C82769 from the DDBJ database. The nucleotide sequence for an SH2A-like gene from *Drosophila* is provided by accession AI517276 from the Genbank database. Three different SH2A-like genes in *Caenorhabditis elegans* are provided by accessions Z68116 from the EMBL database, U80455 from the EMBL database, and U23173 from the EMBL database.

Accession Z48613 from the EMBL database provides the nucleotide sequence for a *Saccharomyces cerevisiae* SH2A-like gene. Accession AA783142 from the Genbank database provides the nucleotide sequence for an SH2A-like gene from *Emericella nidulans*. Accession AL033388 from the EMBL database provides the nucleotide sequence for a *Schizosaccharomyces pombe* SH2A-like gene. Accession Z99111 from the EMBL database provides the nucleotide sequence for a *Bacillus subtilis* SH2A-like gene. Accession AE000766 from Genbank provides the nucleotide sequence for an SH2A-like gene from *Aquifex aeolicus*. Accession P28809 from the SWISS-PROT database provides the protein sequence for an SH2A-like gene from *Pseudomonas aeroginosa*.

Applicants respectfully submit that the presently pending claims are not directed to SH2A and SH2A-like nucleic acid sequences *per se*, but to transgenic cells and plants which have been transformed with an SH2A or SH2A-like gene. Thus, the present invention lies in part, on the discovery that such SH2A sequences may be used in conferring useful phenotypes on transgenic host cells, including plant cells.

The Federal Circuit's findings in *University of California v. Eli Lilly and Co.* 119 F.3d 1559, 1568, 43 USPQ2d 1398 (Fed. Cir. 1997) are not relevant to the present application. In *U.C. v. Lilly*, the patent holder had obtained claims directed in part to a nucleotide sequence encoding human insulin. The specification exemplified a rat insulin cDNA and described a method of obtaining the human insulin gene sequence by referring to a general method for obtaining the human cDNA along with the amino acid sequences of human insulin A and B chains. No sequence information for a human cDNA appeared in the patent. The Federal Circuit found that whether or not the specification provided an enabling disclosure, the patent did not provide a written description of the cDNA encoding human insulin. In contrast, as discussed thoroughly above, in addition to the two rice sequences provided by the present application, the present application provides no less than 26 different SH2A-like genes, either by setting forth the sequence in the Sequence Listing of the present application or by providing an accession number whereby one skilled in the art could obtain the corresponding SH2A-like gene through a public genetic database. Withdrawal of the rejection of claims 1-2, 4-8, 25-29, and 33-36 under the written description requirement of the 35 U.S.C. §112, first paragraph, is therefore warranted.

Claims 1-2, 4, 6, 8, 25-29 and 33-36 including claims 5 and 7 dependent thereon, have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out an distinctly claim the subject matter which applicant regards as the invention. According to the Examiner, the rejected claims are indefinite in the recitation of "SH2A or SH2A-like" and that it is unclear what the acronym "SH2A" designates. Applicants direct the examiner's attention to the paragraph bridging pages 8 and 9 of the specification where the offending term is clearly defined:

> The present invention provides an SH2A gene and corresponding SH2A protein from rice. The present invention also provides SH2A-like genes and SH2A homologs from various organisms. As used herein, the terms "SH2A-like gene" and "SH2A or like gene" refer to a gene from an organism other than rice (*Oryza sativa*) which corresponds to the SH2A gene in rice as exhibited by homologous nucleotide sequence. The terms "SH2A-like protein" and "SH2A homolog" refer to a protein homologous to SH2A in an organism other than rice as exhibited by homologous amino acid sequence and the function of conferring adaptation and/or growth under hypoxic conditions. Thus the present invention is directed to SH2A and its derivatives, homologs and functional analogs. Use herein of the term "SH2A or like protein" encompasses all such homologous or heterologous derivatives, homologs, and functional analogs. The SH2A and SH2A-like genetic sequence and corresponding protein may be homologous to a particular cell, i.e., is naturally occurring in such cell or may be heterologous to the cell, i.e., the genetic sequences or protein may be introduced into the cell from a source not originating with the same organism.

Applicants respectfully submit that SH2 is likely to stand for "subtractive hybridisation clone 2" since the SH2 gene was isolated by this method. *See* Example 2 of the present application. SH2 and SH2-like genes in the public databases are presently called (SIP2) Submergence Induced Protein 2, and have recently been renamed in the literature as *Os*ARD1 and *Os*ARD2, with 'ARD' standing for Acid-Reductone Dioxygenase.

In determining whether claims comply with the second paragraph of section 112, a determination is first made as to whether the claims "set out and circumscribe a particular area with a reasonable degree of precision and particularity." *In re Moore*, 39 F.2d 1232, 169 USPQ 23 (CCPA 1971). The claims should not be considered in a vacuum, "but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertaining art." *Id.* It is respectfully submitted

that claims 1-2, 4-8, 25-29 and 33-36 set out and circumscribe a particular area with a reasonable degree of precision and particularity, namely sequence homology and function, when considered in light of the teachings of the prior art and the specification.

Claims 1-2 and 33-36 are alleged to be indefinite in the recitation of "essentially derived". Applicants direct the Examiner's attention to page 37, penultimate paragraph, where a definition for the term "essentially derived" is provided: "[a]s used herein, an 'essentially derived variety' is held to exist where (a) it is predominantly derived from the initial variety, (b) it is distinct from the initial variety and (c) it conforms essentially to the initial variety in the expression of the introduced transgene." The Examiner's position is that "it is unclear what characteristics of the transgenic plant would be retained by an "essentially derived" variety. Office Action, page 5. The definition for an essentially derived variety provided in the specification states that "it conforms essentially to the initial variety in the expression of the introduced transgene." As presently amended, claim 1 and claims 33-36 dependent thereon, recite in relevant part: "[a] transgenic plant having an altered ethylene response or an essentially derived variety thereof...wherein said nucleotide sequence is heterologous to the genome of said transgenic plant, essentially derived variety thereof..." As presently amended, claim 2 and claims 33-36 dependent thereon recite in relevant part: "[a] transgenic plant having an altered ethylene response or an essentially derived variety thereof...wherein said nucleotide sequence has been introduced into the transgenic plant, plant part or plant cell by recombinant DNA means." Thus, from the definition provided in the specification and the presently amended claims, it is evident that the altered ethylene response would be retained by the essentially

derived variety of a transgenic plant comprising a heterologous nucleotide sequence for an SNA2A or SH2A-like gene.

Based on the foregoing discussion, withdrawal of the rejection of claims 1-2, 4-8, 25-29 and 33-36 under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 33-36 have been rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. As presently amended, Claims 33-36 recite that the pollen, seed, cuttings and flowers comprise the SH2 or SH2A-like gene introduced into the transgenic plant. Withdrawal of the rejection of claims 33-36 under 35 U.S.C. §101 is therefore respectfully requested.

Claims 1-2, 4-8, 25-29 and 33-36 have been rejected under 35 U.S.C. §101 as allegedly not supported by either a specific and substantial asserted utility or a well established utility. The same claims have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly directed to non-enabled subject matter. According to the Examiner, the rejected claims do not recite a specific function for the SH2A gene or the polypeptide it encodes. Applicants traverse the rejection and respectfully submit the following. As presently amended, claims 1 and 2 recite in relevant part: "[a] transgenic plant having an altered ethylene response." According to the Examiner, '[a]lthough the specification reveals that the DNA sequence of SEQ ID NO:1 encodes a polypeptide having amino acid sequence homology to putative proteins and ORRFs of a number of ESTs corresponding to hypothetical proteins of other plants, animals, and fungi, as well as to bacterial proteins, no empirical data is provided to support a function for the protein encoded by SEQ ID NO:1." Office Action, page 6. Applicants direct the Examiner to page 2, lines 6-8, of the specification where it is disclosed that "the subject SH2 genes are responsible

for the induction of anaerobiosis-induced SH2 proteins and hence for one of the most basic mechanisms in adaptation to hypoxic conditions." Applicants further submit that such evidence for the role of SH2 genes is provided by the present application in the submergence responsive expression experiments for SH2A and SH2B. *See* e.g., Example 4. More information is provided in Example 6 where it is disclosed that the SH2A gene is regulated by ethylene. Thus, empirical data is provided by the present application and was used in assigning a function to the SH2A protein of the invention, as shown in Example 4.

The examiner also asserts that function assignment based on homology to other known proteins is supposedly unreliable and cites a reference in the name of Doerks *et al.* (TIG June 1998 Vol. 14 No. 6). Applicants respectfully submit that the assignment of a function to the SH2A protein of the invention was not done solely by considering homology. Even if it had been, the document cited by the examiner appears to be somewhat outdated in this fast-moving field of biotechnology. The document in the name of Doerks *et al* was published in 1998, a whole three years before the filing date of the present invention. The Examiner will no doubt be well aware that in this fast-moving field much progress can be made within the space of three years. This means that with improving technology, and given the ever continuous updating of databases, it is highly probable that the database entries at the time of filing of the application were more complete and reliable than they might have been at the time of publication of the reference in the name of Doerks *et al.* Furthermore, given the highly conserved nature of the sequences of the invention, Applicants submit that the homologues defined in the present application are correct. Moreover, the fact that those skilled in the art continue today to use these techniques to assign homology despite what is said in the Doerks *et al.* document is strong

proof contrary to the Examiner's position. Applicants respectfully submit that Doerks et al. is more a warning to use the correct tools and does not discourage the proper use of databases for the functional assignment of homology.

On Page 7 of the Office Action, the Examiner states that the claimed plants, cells and constructs lack substantial utility under the current guidelines. The Examiner states that while the specification implies that the SH2A gene is useful because it encodes a protein that may function to confer adaptation to hypoxic conditions when expressed in plants, the specification does not disclose any function for the sequence encoded by SEQ ID NO: 1. Applicants submit that as discussed thoroughly above, the specification *does* describe a function for the sequence encoded by SEQ ID NO:1. As described *supra*, the subject SH2A genes are responsible for the induction of anaerobiosis-induced SH2 proteins and hence for one of the most basic mechanisms in adaptation to hypoxic conditions.

The Examiner further alleges that the Applicant does not teach how the claimed plants, cells and constructs would be substantially beneficial to the public, although the examiner does admit that plants, cells and constructs comprising nucleotide sequences encoding proteins of known function may have a well established utility. Since the protein of the invention has a clear function, it is respectfully submitted that the Examiner's position is in error.

The Examiner further objects that "It is apparent that extensive further research, not considered to be routine experimentation, would be required before one of skill in the art would know how to use the claimed invention." It is respectfully submitted that ample guidance is provided in the specification defining homologues of the SH2A protein/gene and defining methods on how to search for further homologues. The specification also details the

transformation of plants and other organisms with the SH2A gene or homologue thereof. *See e.g.*, Examples 9, 10, 11 and 13. Methods for the evaluation of transformed plants are also detailed in Examples 12 and 15. Even though extensively detailed in the specification, methods for searching for homologues of a particular nucleotide or amino acid sequence, methods for transformation, and methods for evaluating plants tolerant to hypoxia are well known in the art and can be performed using known techniques and do not require the exercise of inventive skill.

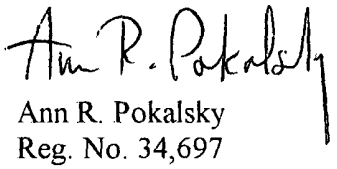
It is respectfully submitted that the present application teaches a specific, and substantial asserted utility. Summarizing, the present application teaches that modulating the expression and/or activity of SH2A or SH2A-like protein in a cell allows growth of the cell in conditions of low oxygen. *See* specification, page 2, lines 8-10. Specifically with respect to plants, the present application also teaches the presently claimed transgenic plants having an altered ethylene response. *See* specification, page 27, lines 17-24. Evidence for such specific and substantial asserted utility is provided in the specification by Examples 4 and 6.

Only one specific, substantial and credible utility is required to satisfy the statutory requirement. Utility Guidelines, *Fed. Reg. Vol.* 66, No. 4, Friday, January 5, 2001, Notices, page 1098. "Only where the totality of the record *continues* to show that the asserted utility is not specific, substantial, and credible should a rejection based on lack of utility be maintained." Utility Guidelines, page 1099. In addition, since Applicants have now rebutted a rejection based on allegedly lack of utility under section 101, the corresponding rejection imposed under section 112 should also be withdrawn. *Id.* Based on the foregoing, withdrawal of the rejection of Claims 1-2, 4-8, 25-29 and 33-36 under 35 U.S.C. §§101 and 112, first paragraph is respectfully requested.

Claims 6 to 8 and 25 to 28 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Choi et al. (1994 *Mammalian Genome* 5(1):52-54. Applicants traverse the rejection and respectfully submit the following. Choi et al. describe a histone protein, with the designation 'sH2A' denoting a Histone Somatic protein. Choi et al also teach a genetic construct comprising the sH2A gene. According to the Examiner, since the sH2A gene was obtained from a bacteriophage library, the nucleotide sequence taught by Choi et al. would necessarily have been contained in a bacterial host cell. In contrast, the host cells recited in claims 6-8 and the genetic construct recited in claims 25-28 are *not* directed to a sequence encoding a histone protein, but rather to a gene responsible for the induction of anaerobiosis-induced SH2 proteins as defined by the present specification. Applicants' invention recited in claims 6-8 and 25-28 is thus distinguished over the disclosure of Choi et al. Withdrawal of the rejection of claims 6-8 and 25-28 under 25 U.S.C. §102(b) is therefore warranted.

In view of the amendments to the claims and the foregoing remarks, it is respectfully submitted that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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